Agence de réglementation de la lutte antiparasitaire
Pest Management Regulatory Agency

Proposed Acceptability for Continuing Registration

PACR2007-04

Re-evaluation of Chlorpropham

The purpose of this document is to inform registrants, pesticide regulatory officials and the Canadian public that Health Canada's Pest Management Regulatory Agency (PMRA) has re-evaluated chlorpropham under the authority of the *Pest Control Products Act*. This Proposed Acceptability for Continuing Registration document provides a summary of the data and information reviewed and the rationale for the proposed regulatory decision.

The PMRA has determined that the use of chlorpropham and its end-use products does not entail an unacceptable risk to human health and the environment, provided that the proposed mitigation measures to further protect workers are implemented.

By way of this document, the PMRA is soliciting comments from interested parties on the proposed regulatory decision for chlorpropham. The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed decision. All comments should be forwarded to Publications at the address below.

(publié aussi en français)

26 March 2007

This document is published by the Alternative Strategies and Regulatory Affairs Division, Pest Management Regulatory Agency. For further information, please contact:

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ISBN: 978-0-662-45703-9 (978-0-662-45704-6)
Catalogue number: H113-18/2007-4E (H113-18/2007-4E-PDF)

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Foreword

The available information for the active ingredient chlorpropham and the associated end-uses on potatoes has been re-evaluated by Health Canada's Pest Management Regulatory Agency (PMRA). The registrants of the technical class products are Brenntag Canada Inc., Decco Cerexagri Inc. and Aceto Agricultural Chemicals.

The PMRA announced on 29 August 2002 that certain carbamate active ingredients and their associated end-use products, including chlorpropham, were subject to re-evaluation[1].

The PMRA has carried out an assessment of available information and has concluded that the use of chlorpropham and its end-use products does not entail an unacceptable risk to human health and the environment, provided that the proposed mitigation measures to further protect workers are implemented.

The PMRA will accept written comments on this proposal up to 60 days from the date of this document to allow interested parties an opportunity to provide input into the proposed re-evaluation decision for these products.

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1 See Re-evaluation Note REV2002-06, *Re-evaluation of Selected Carbamate Pesticides*.

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1.0 Purpose

The purpose of this document is to inform registrants, pesticide regulatory officials and the Canadian public that Health Canada's Pest Management Regulatory Agency (PMRA) has re-evaluated chlorpropham. The document includes a human health risk assessment, an environmental risk assessment and information on the uses of chlorpropham. By way of this document, the PMRA is soliciting comments from interested parties on the proposed regulatory decision for chlorpropham.

2.0 Re-evaluation of Chlorpropham

Chlorpropham is one of the pesticides subject to re-evaluation in Canada as announced in Re-evaluation Note REV2002-06, *Re-evaluation of Selected Carbamate Pesticides*. Chlorpropham is a carbamate pesticide that inhibits mitosis. It is registered in Canada as a potato sprout inhibitor and works by systemic action.

2.1 Identity of the Active Substance and the End-Use Products Containing It

Active substance: Chlorpropham

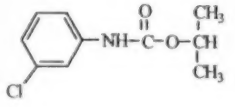
Chemical name:

IUPAC	Isopropyl 3-chlorocarbanilate
CAS	1-methylethyl (3-chlorophenyl) carbamate

Chemical class: Carbamate

CAS number: 101-21-3

Structural formula:



Impurities of toxicological concern, as per Regulatory Directive DIR98-04, *Chemistry Requirement for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*, or Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, are not expected to be present in the starting materials used to manufacture the product nor are they expected to be formed during the manufacturing process.

2.2 Description of Registered Chlorpropham Uses

Appendix I lists all the products containing chlopropham currently registered in Canada. Appendix II lists all the uses for which chlorpropham is presently registered (Use-Site Category 12: Stored Food and Feed). All uses are supported by the registrants.

3.0 Effects Having Relevance to Human Health

3.1 Toxicology Summary

Toxicokinetic assays indicate that chlorpropham is readily absorbed following oral exposure to the rat. Chlorpropham metabolites in rats appear to be distributed to most major organs, with the greatest concentrations being observed in the liver, kidney, intestines, spleen and blood. Chlorpropham crosses the blood-brain and placental barriers in rats.

Extensive metabolism occurs rapidly. As many as 21 metabolites are formed through three metabolic pathways, with the principal pathway resulting in the p-hydroxylation of the phenyl ring. p-Hydroxychlorpropham and its conjugates are the major metabolites identified in urine following oral or intraperitoneal dosing. m-Chloroaniline and its conjugates are formed through the secondary metabolic pathway. The formation of chlorpropham alcohol and its conjugates represent the tertiary pathway.

Following oral exposure, peak excretion occurs rapidly with minimal retention. Excretion is primarily through the urine with lesser amounts eliminated in exhaled air and feces. Studies also indicate that chlorpropham metabolites are able to be transferred by maternal milk in rats.

Chlorpropham is of low oral toxicity through oral and dermal routes of exposure. The requirement for inhalation studies has been waived because chlorpropham cannot be prepared in a respirable manner for the purposes of toxicity studies. No route-specific effects are anticipated. Chlorpropham is mildly irritating to the eyes and to the skin. It is not a skin sensitizer.

Repeat-dose studies suggest that chlorpropham targets primarily the hematological system with effects related to hemolytic anemia and methemoglobinemia being consistently observed throughout oral short- and long-term mouse, rat and dog studies.

Hemolytic anemia is characterized by reductions in various hematological parameters including red blood cell counts, hematocrit and hemoglobin concentrations. Treatment-related effects on organ weight, gross pathology and histopathology of the spleen, liver and bone marrow have also been observed in species dosed with chlorpropham. Compensatory hematopoiesis related to the anemic effects of chlorpropham has also been commonly observed in spleen, liver and bone marrow.

Methemoglobin results from the oxidation of the ferrous group in hemoglobin, preventing the red blood cells from acting as effective oxygen carriers. Methemoglobinemia occurs once cardiovascular adaptations can no longer compensate for the oxygen shortage and is characterized clinically by darkened blood, hypoxia, cyanosis and dyspnea.

Clinical symptoms are associated with methemoglobin levels of 10%. Effects related to the administration of chlorpropham were considered adverse when methemoglobin concentrations met or exceeded 10% of total hemoglobin or were accompanied by adverse effects on the hematopoietic system. A subchronic study in which rats were treated orally with chlorpropham

indicates that a 10% level of methemoglobin is likely to be observed only at oral dose levels significantly greater than those that cause splenic toxicity.

There was no evidence of cholinesterase inhibition or delayed neurotoxicity in the available studies.

Although less sensitive to the hematological effects of chlorpropham, dogs were the most sensitive of test species examined for endocrine effects following repeat oral exposures. Treatment-related endocrine effects appear to target primarily the thyroid gland in dogs and the testes in rats.

Negative results have been obtained in an in vivo micronucleus assay as well as most in vitro mutagenicity and clastogenicity assays identified. Chlorpropham is unlikely to be mutagenic or clastogenic, although studies suggest that it may cause aneuploidy.

There were no indications of carcinogenesis in a mouse carcinogenicity bioassay. Benign Leydig cell tumours were present at the limit dose in a rat carcinogenicity bioassay, accompanied by excessive toxicity to the animals. There were no studies investigating the mechanism of the chlorpropham induced Leydig cell tumours identified; however, available evidence suggests that structural analogues of both chlorpropham and p-hydroxychlorpropham including flutamide, linuron and procymidone may cause Leydig cell tumours in rats through an anti-androgenic mechanism. Although the increase in Leydig cell tumours in the rat study is believed to be treatment-related, it was only present at a dose level that exceeded the maximum tolerated dose. Current data suggest that chlorpropham does not pose a carcinogenic risk to the general population.

In a two-generational reproductive toxicity assay, maternal toxicity was observed as splenic effects at the lowest dose tested, with reproductive and developmental effects occurring only at higher doses. There were no indications of teratogenic effects in rats or rabbits. The only developmental toxicity observed was an increase in postimplantation loss and delayed ossification in rabbits at maternally toxic dose levels. The evidence available suggests that the young do not have an increased sensitivity to chlorpropham.

Reference doses have been set based on no observed adverse effect levels (NOAELs) for the most sensitive indicators of toxicity, namely the endocrine system. These reference doses incorporate various uncertainty factors to account for extrapolating between laboratory animals and humans and for variability within the human population. Additional safety factors were also warranted in order to account for endpoints of concern.

The toxicology endpoints used in the risk assessment of chlorpropham are summarized in Appendix III.

3.2 Occupational and Residential Risk Assessment

Workers can be exposed to chlorpropham through mixing, loading or applying the end-use products, or when re-entering a treated site. Occupational scenarios resulting in operator exposure are limited to the application of chlorpropham to postharvest potatoes.

Occupational risk is estimated by comparing a calculated margin of exposure (MOE) to a target MOE incorporating safety factors protective of the most sensitive subpopulation. MOEs greater than or equal to the target MOE do not require risk mitigation. For chlorpropham, the toxicological endpoint of effects on the thyroid gland is considered relevant to all exposure routes. Thus, it is appropriate to combine the route-specific exposures to generate a single risk estimate.

Usually, for workers entering a treated site, restricted entry intervals are calculated to determine the minimum length of time required before workers or others can safely re-enter. No data exist to adequately assess exposure during postapplication activities following application of chlorpropham to storage potatoes. Consequently, postapplication risk is addressed through the use of personal protective equipment (PPE), as described in Section 3.2.2.

For short- and intermediate-term dermal risk assessment, the results of a 90-day oral (capsule) study in the dog was selected. A no observed adverse effect level (NOAEL) of 25 mg/kg bw/day was established based on various effects on the thyroid gland at the next highest dose level of 125 mg/kg bw/day. The target MOE selected for this study is 300 accounting for standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability as well as an additional safety factor of threefold for effects on the endocrine system. The selection of this study and MOE is considered to be protective of all populations including pregnant women and their unborn children.

The same study and target MOE was selected for short- and intermediate-term inhalation risk assessment as there were no repeat-dose inhalation studies available.

3.2.1 Mixer/Loader/Applicator Exposure and Risk Assessment

There are potential exposures to mixers, loaders, applicators or other handlers (baggers/packers). Based on typical use pattern, the major scenarios identified were as follows:

- mixing/loading solutions/solids to be applied to storage potatoes by foggers (large scale storage facilities); and
- mixing/loading/applying emulsifiable concentrates to storage potatoes as a spray (smaller storage/packing facilities).

Based on the number of applications (1–2) and the nature of the applications, workers applying chlorpropham have a short (1–30 days) to intermediate (1–3 months) duration of exposure.

No chemical-specific handler exposure data were submitted for chlorpropham; therefore, daily dermal and inhalation handler doses were estimated using data from the Pesticide Handlers

Exposure Database (PHED), Version 1.1. The PHED is a compilation of generic mixer/loader applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of PPE.

Mixer/loader/applicator exposure estimates are based on the best available data at this time. The assessment might be refined with exposure data more representative of modern application equipment and engineering controls. Biological monitoring data could also further refine the assessment.

The PMRA estimated handler exposure based on the following level of PPE:

- Mid-level PPE—cotton coveralls over a single layer and chemical-resistant glove, with open mixing and loading for spray application and closed mixing and loading for foggers

At this time, only mixer/loader risk assessments could be conducted for the closed system in the larger storage facilities. Applicator exposure could not be characterized, as data do not exist to adequately assess exposure from applicator activities. However, due to the closed and automated nature of the systems, applicator exposure is expected to be minimal.

Worker exposure for the treatment of potatoes on conveyers/rollers in smaller facilities was estimated using PHED data for low-pressure handwand application. The treatment of potatoes on conveyers is done using multiple nozzles, from above, below, or both directions, spraying droplets evenly over the potatoes as they are moved to storage (or to bagging). Some delivery systems do not employ a closed method of application; instead, barriers or screens are constructed to minimize drift as spray is directed at the potatoes as they move along the rollers/conveyer belts. At this time, data are not available to assess exposure to workers during the treatment of stored potatoes or potatoes entering storage. Although low-pressure handwand data are not appropriate to estimate the exposure in this scenario, it is considered a highly conservative estimate for the following reasons:

- the application to potatoes on rollers/conveyers is screened, minimizing drift, whereas drift onto applicators from low-pressure handwands can be significant;
- unlike handwand applications, workers in the potato facilities are only responsible for mixing and loading the product, and the application is done automatically; and
- unlike handwand applications, nozzles in the potato facilities are fixed and directed only at the conveyers/rollers.

Occupational risk estimates associated with application, mixing and loading for all current label uses are acceptable, provided PPE is used (see Appendix IV).

3.2.2 Postapplication Exposure and Risk Assessment

No data exist to adequately assess exposure during postapplication activities following application of chlorpropham to storage potatoes.

There is potential for both dermal and inhalation exposure for workers filling potato sacks after potatoes have been treated on the rollers/conveyer belts in smaller facilities. Most potatoes that are treated are bound for storage and will not be bagged until they have been processed later at a treatment facility. In certain facilities, some potatoes will not be treated at all and will be sent straight to retailers. In other scenarios, potatoes will be treated just before they are bagged in order to prolong their ability to avoid sprouting during shipping to retail. In these scenarios, there is potential for dermal exposure (and to a degree, inhalation exposure) from handling potatoes that have been recently treated. To mitigate the risk, workers must wear cotton coveralls and chemical-resistant gloves.

There is potential for both postapplication dermal and inhalation exposure to workers entering storage areas that have been treated with chlorpropham. The cleaning of equipment, fans, fan guards, plenum and other surfaces in contact with the chemical represents a potentially high exposure scenario. Although there are no data to assess exposure during postapplication activities, the potential for exposure requires that the worker wear maximum PPE for certain postapplication activities (see Section 6.2).

Products that are designed specifically for large-scale fogging use also have specific label recommendations for the use of ventilating fans following a treatment. The product labels state that a minimum of 2–4 hours of ventilation is required before entering a treated area. These same recommendations should be included on any label for a product that could be used in a large scale storage facility.

3.2.3 Residential Exposure and Risk Assessment

As chlorpropham is not currently registered for use in any residential areas, a residential risk assessment was not performed.

3.3 Dietary Risk Assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in fruits, vegetables, milk, meat, eggs and processed products, may be ingested with the daily diet. These dietary assessments are age-specific and incorporate the different eating habits of the population at various stages of life (infants, children, adolescents, adults and seniors). For example, assessments take into account children's greater consumption of fruit, vegetables and juices for their body weight compared with adults.

Acute dietary risk was calculated using food consumption and food residue data. A deterministic analysis was performed considering the Continuing Survey of Food Intakes by Individuals (CSFII) food consumption values and maximum residue levels to estimate the potential daily intake (PDI) of chlorpropham residues. An exposure value representing the 95th percentile PDI is compared with the acute reference dose (ARfD), which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the PDI is less than the ARfD, the intake is not considered to be of concern.

The acute dietary exposure was calculated using American tolerances for meat and meat byproducts, the Canadian general maximum residue limit (MRL) for spinach imported from the United States, the maximum value from the Canadian Food Inspection Agency monitoring data for potatoes and default processing factors for processed potato fractions from the Dietary Exposure Evaluation Model (DEEM™) Version 7.87.

An ARfD for the general population including children was not established because no endpoint attributable to a single exposure was identified in the available toxicity studies.

To estimate acute dietary risk (1 day) for females of child-bearing age, the developmental toxicity study in rabbits was selected for risk assessment. At a dose of 500 mg/kg bw/day, a significant increase in postimplantation loss was observed in the presence of maternal toxicity. A NOAEL of 250 mg/kg bw/day was established. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability as well as an additional safety factor of threefold due to the severity of endpoint of postimplantation loss (embryofetal death) are used. The ARfD was calculated to be 0.83 mg/kg bw.

Acute dietary risk from foods treated with chlorpropham was not a concern for any subpopulation of females of child-bearing age. At the 95th percentile of exposure, the PDI for the most highly exposed population subgroup, nursing females (13+), was 17% of the ARfD. All other female subpopulations had potential dietary intakes less than 17% of the ARfD.

The chronic dietary risk is calculated on the basis of the average consumption of different foods and average residue values on those foods. The expected intake of residues is compared with the acceptable daily intake (ADI), which is the dose that an individual could be exposed to over a lifetime and expect no adverse health effects. When the expected intake from residues is less than the ADI, the expected intake is not considered to be of concern.

Chronic dietary exposure was calculated using a deterministic assessment. Values for commodities on which chlorpropham may be found in Canada and the United States were incorporated into the assessment by using the mean residue for potatoes from the Canadian Food Inspection Agency monitoring data, American tolerances for meat and meat byproducts, the Canadian general MRL for spinach imported from the United States, and default processing factors for processed potato fractions from DEEM™, Version 7.87.

To estimate dietary risk from the repeat or chronic exposure, the NOAEL of 5 mg/kg bw/day from the 60-week oral dog study was selected for risk assessment. The NOAEL is based on thyroid effects at the lowest observed adverse effect level (LOAEL) of 50 mg/kg bw/day. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability are used. An additional safety factor of threefold due to effects on the endocrine system is also included. The ADI was calculated to be 0.02 mg/kg bw/day (5 mg/kg bw/day ÷ 300). This value was considered to be protective of all populations including infants and children.

Chronic dietary risk from foods is not a concern for the general Canadian population and all population subgroups. The most highly exposed population subgroup, children (1–2 years), consume 66% of the ADI.

3.4 Drinking Water Exposure

As chlorpropham is only registered for indoor, postharvest use on stored potatoes in Canada, there is minimal potential for exposure via drinking water.

3.5 Aggregate Exposure Assessment

Aggregate risk assessment looks at the combined potential risk associated with exposures from food, drinking water and residential uses of a pesticide. As there are no residential uses of chlorpropham and drinking water exposure is not expected, aggregate risk is below the level of concern based on the acceptable acute and chronic dietary risk assessments (see Section 3.3).

4.0 Environmental Assessment

This assessment is based on data from the following sources:

- the United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) document (EPA 738-R-96-023, October 1996);
- the Netherlands National Institute of Public Health and Environmental Protection (NIPHEP) review of chlorpropham (88/678801/106, June 1989);
- the European Union review report for chlorpropham (November 2003);
- the Extoxnet (Extension Toxicology Network) database; and
- the *e-Pesticide Manual*, 12th edition (2002–2003).

4.1 Environmental Fate

Chlorpropham is highly soluble (89 mg/L at 25°C) in water. The *n*-octanol–water partition coefficient (log K_{ow}) of 3.4 indicates that chlorpropham has potential for bioaccumulation. Chlorpropham has a vapour pressure of 2.4×10^{-2} Pa at 20°C, indicating that it is not volatile. The Henry's law constant (4.64×10^{-7} atm·m^3·mole^{-1}) indicates that chlorpropham is not volatile from moist soil and water surface.

Available data indicate that chlorpropham is slightly to moderately persistent in the environment. Laboratory studies reported half-lives of chlorpropham ranging from 22 to 65 days under aerobic conditions. Under field conditions, chlorpropham is expected to be moderately mobile in soil (K_{oc} = 260–480). A column leaching study shows no parent compound in leachate after 35 days, indicating that chlorpropham has a low potential for leaching.

Chlorpropham is stable to hydrolysis under environmentally relevant pHs (dissipation time 50% > 1 year). The reported field half-life of chlorpropham phototransformation in the water is 83 days. Reported half-lives of chlorpropham ranged from 18 to 39 days and from 44 to

145 days in water and water/sediment system, respectively, indicating that chlorpropham is slightly to moderately persistent in water.

4.2 Environmental Toxicology

Chlorpropham is non-toxic to honeybees (LD_{50} = 466 µg/bee), birds (LD_{50} > 2000 mg/kg bw) and mammals (LD_{50} = 4200 mg/kg) on an acute basis. It is also non-toxic to birds and mammals on a chronic basis, the no observed effect concentration (NOEC) being ≥1000 mg/kg. Chlorpropham is moderately toxic to aquatic invertebrates (LC_{50} = 2.6–4.0 mg/L), fish (LC_{50} = 5.5–7.3 mg/L), algae and plants (EC_{50} = 1.67 mg/L).

4.3 Concentrations in Drinking Water

The potential for the contamination of drinking water with chlorpropham is expected to be minimal because the current registered use pattern in Canada is not expected to result in any exposure to soil that could lead to runoff into surface waters or leaching to groundwater. Chlorpropham is used only on potatoes moving along the packing line, prior to packing into shipping boxes. In view of the limited use pattern, environmental exposure is expected to be minimal.

4.4 Terrestrial Risk Assessment

The terrestrial environmental risk was not conducted due to the use pattern, indicating that the exposure of non-target terrestrial organisms will be minimal.

4.5 Aquatic Risk Assessment

The aquatic environmental risk was not conducted. Due to the use pattern, the exposure of non-target aquatic organisms to chlorpropham is not expected.

4.6 Environmental Assessment Conclusions

The use pattern indicates that chlorpropham will not pose a risk to terrestrial and aquatic non-target organisms because the exposure of non-target terrestrial and aquatic organisms to chlorpropham will be minimal.

5.0 Other Assessment Considerations

5.1 Toxic Substances Management Policy

During the review of chlorpropham, the PMRA has taken into account the federal Toxic Substances Management Policy[1] and has followed its Regulatory Directive DIR99-03[2]. It has been determined that this active ingredient does not meet the TSMP Track 1 criteria for the following reasons.

- Its values for half-life in water (≤ 39 days) and soil (≤ 65 days) are below the TSMP Track 1 cut-off criteria for water (≥ 182 days) and soil (≥ 182 days). Therefore, it does not meet the criteria for persistence.

- The log K_{ow} is 3.4, which is below the TSMP Track 1 cut-off criterion of ≥5.0. Therefore, it is not bioaccumulative.

- Its technical grade active ingredient does not contain any byproducts or microcontaminants that meet the TSMP Track 1 criteria. Impurities of toxicological concern are not expected to be present in the raw materials nor are they expected to be generated during the manufacturing process.

- The formulated products do not contain any formulants that are known to contain TSMP Track 1 substances.

The toxicity of chlorpropham is described in sections 3.0 and 4.2.

5.2 Formulant Issues

Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Program and Implementation Guidance Document*, published on 31 May 2006.

6.0 Proposed Regulatory Actions

The PMRA has determined that the dietary and drinking water risks, worker risks during mixing, loading and application and postapplication as well as risks to the environment are acceptable, provided that the mitigation measures listed below are implemented.

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1 The federal Toxic Substances Management Policy is available through Environment Canada's website at www.ec.gc.ca/toxics.

2 Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, is available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra_infoserv@hc-sc.gc.ca; or through our website at www.pmra-arla.gc.ca.

6.1 Proposed Regulatory Actions Relating to Toxicology

Labels of pesticide products carry statements regarding symptoms of poisoning and treatment, which are especially important for those who may be overexposed when working with the product in a commercial or industrial setting, e.g., mixers/loaders who handle more concentrated forms. Based on the toxicological assessments, the label text of the chlorpropham-containing products should be expanded and/or standardized to include the following toxicological information:

"Overexposure to chlorpropham may result in methemoglobinemia."

6.2 Proposals Pertaining to Mixer/Loader/Applicator and Postapplication Exposure

All mixing, loading and applying scenarios assessed meet the target MOE of 300 using mid-level PPE. There are insufficient data to assess all application and postapplication exposure scenarios.

Due to the possibility of exposure during application or postapplication activities, it is recommended that maximum PPE be worn for certain activities. Maximum PPE is required because exposure cannot be quantified at this time and certain postapplication scenarios represent potentially high exposure scenarios. Labels should be amended to include the following recommendations for PPE (if not already stated):

A. For mixing and loading:
"Wear cotton coveralls and chemical-resistant gloves."

B. For application using the screened sprayer systems and for bagging/packing potatoes:
"Wear cotton coveralls and chemical-resistant gloves."

C. In facilities using closed fogger systems:
   1. For all re-entry tasks (including cleaning) prior to the completion of ventilation:
   "Wear chemical-resistant coveralls over a long-sleeved shirt and pants, chemical-resistant gloves and a self-contained breathing apparatus."

   2. For cleaning following ventilation:
   "Wear chemical-resistant coveralls over a long-sleeved shirt and pants, chemical-resistant gloves and a suitable respirator."

   3. For tasks other than cleaning following ventilation:
   "Wear cotton coveralls and chemical-resistant gloves."

D. For products that could potentially be used in large scale foggers must include following explicit label instructions regarding ventilation and restricted entry intervals:
"Do not allow entry into treated areas (to attend to fans, etc.) until two hours of mechanical ventilation (fans should circulate outside air) or four hours of passive ventilation (windows, vents and doors should be opened) have occurred."

E. Chlorpropham products that are applied by spray on a conveyor belt must state on the label:
"Installation of a shield around the conveyor belt is required to prevent spray mist drifting."

6.3 Proposed Regulatory Actions Relating to Dietary Risk Assessment

The risk from dietary exposure to chlorpropham is acceptable, based on current Canadian and international uses.

6.3.1 Residue of Concern

The existing definition of the residue of concern in Canada is the parent compound chlorpropham (isopropyl 3-chlorocarbanilate).

6.3.2 Maximum Residue Limits for Chlorpropham in Food

In general, when the re-evaluation of a pesticide has been completed, the PMRA intends to update Canadian MRLs and to remove MRLs that are no longer supported. The Agency recognizes, however, that interested parties may want to retain an MRL in the absence of a Canadian registration to allow legal importation of treated commodities into Canada. The PMRA requires similar chemistry and toxicology data for such import MRLs as those required to support Canadian food use registrations. In addition, the Agency requires residue data that are representative of use conditions in exporting countries, in the same manner that representative residue data are required to support domestic use of the pesticide. These requirements are necessary so that the PMRA may determine whether the requested MRLs are needed and to ensure they would not result in unacceptable health risks. Parties interested in supporting an import MRL for residues of chlorproham should contact the PMRA during the comment period of this document to discuss the submission of appropriate data.

Canada currently has an MRL established for residues of chlorpropham on potatoes (15 ppm). Where no specific MRL for a pest control product has been established in the Food and Drug Regulations, subsection B.15.002(1) applies. This requires that residues do not exceed 0.1 ppm and has been considered a general MRL for enforcement purposes.

Residues of chlorpropham in all agricultural commodities other than stored potatoes are regulated by subsection B.15.002(1). However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of the 0.1 ppm General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be promulgated.

6.4 Proposed Regulatory Action Relating to Environment

No environmental risk mitigation is required.

6.5 Proposed Regulatory Action Relating to Value

At this time, no regulatory action is proposed for chlorpropham as a consequence of a value assessment. However, certain label changes are required to clarify intended application rates (Appendix V).

7.0 Proposed Re-evaluation Decision

Health Canada's Pest Management Regulatory Agency has carried out an assessment of available information and has concluded that the use of chlorpropham and its associated end-use products does not entail an unacceptable risk to human health and the environment, provided that the proposed mitigation measures to further protect workers are implemented, i.e., additional PPE and engineering controls. Upon finalization of the re-evaluation decision, the PMRA will provide registrants with specific directions on how to address these measures.

The PMRA will accept written comments up to 60 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed re-evaluation decision for chlorpropham.

List of Abbreviations

µg	microgram
ADI	acceptable daily intake
ARfD	acute reference dose
atm	atmosphere(s)
bw	body weight
CAS	Chemical Abstracts Service
CSFII	Continuing Survey of Food Intakes by Individuals
DACO	data code
DEEM™	Dietary Exposure Evaluation Model
EC_{50}	effective concentration 50%
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{oc}	organic carbon partition coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
m^3	metre(s) cubed
mg	milligram(s)
MOE	margin of exposure
MRL	maximum residue limit
NIPHEP	National Institute of Public Health and Environmental Protection
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
PDI	potential daily intake
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
RED	Reregistration Eligibility Decision
SF	safety factor
TSMP	Toxic Substances Management Policy
UF	uncertainty factor
USC	Use-Site Category
USEPA	United States Environmental Protection Agency

Appendix I Chlorpropham Products Currently Registered (excluding discontinued products) as of 04 December 2005

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
11575	Commercial	Brenntag Canada Inc.	Sprout-NIP EC Potato Sprout Inhibitor	Emulsifiable concentrate or emulsion	350 g/L
11848	Commercial	AG-Services Inc.	Potato Sprout Inhibitor Liquid Concentrate	Solution	500 g/L
18832	Technical	Brenntag Canada Inc.	Chlorpropham Technical	Not applicable or not available	98%
18833	Commercial	Brenntag Canada Inc.	Sprout NIP 840 Sprout Inhibitor for Potatoes	Solution	840 g/L
23680	Technical	DECCO Cerexagri Inc.	CIPC Technical	Solid	99%
24008	Commercial	DECCO Cerexagri Inc.	DECCO 276 EC Potato Sprout Inhibitor	Emulsifiable concentrate or emulsion	25%
24423	Technical	Aceto Agricultural Chemicals	Chloro IPC Technical	Not applicable or not available	98%
24691	Commercial	United Agri Products	Spud-NIC Aerosol Grade	Solution	471 g/L
25834	Commercial	AG-Services Inc.	Ag-Services 750 A "Potato Sprout Inhibitor"	Solution	750 g/L
26927	Commercial	DECCO Cerexagri Inc.	DECCO 271 Potato Sprout Inhibitor	Solid	99%
27213	Commercial	Brenntag Canada Inc.	Sprout NIP 980	Solid	98%
27402	Commercial	AG-Services Inc.	Ag-Services 98A Potato Sprout Inhibitor	Solid	98.7%
27971	Commercial	AG-Services Inc.	Ag-Services Emulsifiable Concentrate	Emulsifiable concentrate or emulsion	350 g/L

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Appendix II Registered Canadian Uses of Chlorpropham

Site(s)	Pests(s)	Marketing Class	Formulation Type	Application Methods and Equipment	Registrant Supports Uses?
USC 12: Stored Food and Feed					
Potato	Sprout inhibition	Commercial	Emulsifiable concentrate or emulsion	Sprayer on packing line	Yes
Potato	Sprout inhibition	Commercial	Solution, solid	Fogging, misting equipment	Yes

Appendix II Registered Canadian Uses of Chlorpropham

Site(s)	Pest(s)	Marketing Class	Formulation Type	Application Method and Equipment	Registered Supported Use?
USC 12: Stored Food and Feed					
Potato	Sprout inhibition	Commercial	Emulsifiable concentrate or emulsion	Sprayer on packing line	Yes
Potato	Sprout inhibition	Commercial	Solution, solid	Fogging, misting equipment	Yes

Appendix III Toxicology Endpoints for Health Risk Assessment for Chlorpropham

Exposure Scenario	Endpoint	Study	NOAEL (mg/kg bw/day)	UF/SF[a] or MOE
Acute dietary	Postimplantation loss	Developmental toxicity rabbit	250	300
Chronic dietary	Thyroid effects	60-week oral dog	5	300
	ADI 0.02 mg kg bw/day			
Short- and intermediate-term[b] dermal[c]	Thyroid effects	90-day oral dog	25	300
Short- and Intermediate-term[b] inhalation[d]	Thyroid effects	90-day oral dog	25	300

[a] UF/SF refers to total of uncertainty and or safety factors for dietary assessments

[b] Duration of exposure is one day to several months

[c] As an oral NOAEL was selected, a dermal absorption factor of 100% should be used in route-to-route extrapolation

[d] As an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) should be used in route-to-route extrapolation

Appendix III Toxicology Endpoints for Health Risk Assessment for Chlorpropham

Exposure Scenario	Endpoint	Study	NOAEL (mg/kg bw/day)	UF/SF[a] or MOE
Acute dietary	Postimplantation loss	Developmental toxicity rabbit	250	300
Chronic dietary	Thyroid effects	60-week oral dog	5	300
	ADI = 0.02 mg/kg bw/day			
Short- and intermediate-term[b] dermal[c]	Thyroid effects	90-day oral dog	25	300
Short- and Intermediate-term[b] inhalation[d]	Thyroid effects	90-day oral dog	25	300

a UF/SF refers to total of uncertainty and/or safety factors for dietary assessments.

b Duration of exposure is one day to several months.

c As an oral NOAEL was selected, a dermal absorption factor of 100% should be used in route-to-route extrapolation.

d As an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) should be used in route-to-route extrapolation.

Appendix IV Indoor Mixer/Loader Exposure Estimates and MOEs With Mid-Level PPE

Crop	Method of Application	Formulation Type	Rate[a] (kg/tonne)	Amount Treated[b] (tonnes)	Daily Exposure[b] (µg/kg/day)		Margins of Exposure		
					Dermal[c]	Inhalation[d]	Dermal[e]	Inhalation[f]	Combined[g]
USC 12: Stored Food and Feed									
Stored potatoes	Fogger	Solution	0.04	6800	37.34	0.43	669	58 489	662
Stored potatoes	Fogger	Solid	0.02	6800	17.86	0.2	1400	126 153	1385
Stored potatoes	Low-pressure handwand	Emulsifiable concentrate	0.01	500	52.52	3.23	476	7743	448

a Maximum label rate.
b Based on crop and equipment specific data.
c Where dermal exposure µg/kg/day = (unit exposure × area treated × rate)/70 kg bw.
d Where inhalation exposure µg/kg/day = (unit exposure × area treated × rate)/70 kg bw.
e Based on a NOAEL of 25 mg/kg/day (from a 90-day oral study in the dog).
f Based on a NOAEL of 25 mg/kg/day (from a 90-day oral study in the dog).
g Combined MOE = $1/(1/MOE_D + 1/MOE_I)$.
h Based on mid-level PPE = cotton coveralls over a single layer of clothing and chemical-resistant gloves with open mixing and loading for low-pressure handwand and closed mixing and loading for foggers.

Appendix IV Indoor Mixer/Loader Exposure Estimates and MOEs With Mid-Level PPE

Crop	Method of Application	Formulation Type	Active (kg/kg)	Amount Treated (tonnes)	Unit Exposure (µg/kg/day)		Margins of Exposure		
									Combined
USC 12: Stored Food and Feed									
Stored potatoes	Fogger	Solution	0.04	6800	37.34	0.43	669	58 489	662
Stored potatoes	Fogger	Solid	0.02	6800	17.86	0.2	1400	126 153	1385
Stored potatoes	Low-pressure handwand	Emulsifiable concentrate	0.01	500	52.52	3.23	476	7743	448

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e Based on a NOAEL of 25 mg/kg/day (from a 90-day oral study in the dog).
f Based on a NOAEL of 25 mg/kg/day (from a 90-day oral study in the dog).
g Combined MOE = $1/(1/MOE_D + 1/MOE_I)$.
h Based on mid-level PPE = cotton coveralls over a single layer of clothing and chemical-resistant gloves with open mixing and loading for low-pressure handwand and closed mixing and loading for foggers.

Appendix V Summary of Label Amendments for Commercial Class Products Containing Chlorpropham

(**Note:** The information presented below does not identify all label requirements for individual end-use products such as first aid statements, disposal statements, precautionary statements and supplementary PPE that may be required. Additional information on labels for currently registered products should not be removed unless it contradicts information in this summary.)

COMMON NAME: Chlorpropham

CHEMICAL NAME: 1-methylethyl (3-chlorophenyl)carbamate

FORMULATION TYPE: Emulsifiable concentrate or emulsion, solution and solid

USE-SITE CATEGORY: USC# 12—Stored Food and Feed

PRIMARY PANEL:

Remove the following statement that, as a result of re-evaluation, is no longer applicable:

> WARNING: Safety data and registration of this product are under review. Directions for use and cautionary statements should be carefully followed.

TOXICOLOGICAL INFORMATION:

All labels should be amended to include the following statement:

> "Overexposure to chlorpropham may result in methemoglobinemia."

PROTECTIVE CLOTHING AND EQUIPMENT:

Engineering Controls:

For chlorpropham products that are applied by spray on a conveyor belt, the following statement must appear on the labels:

> "Installation of a shield around the conveyor belt is required to prevent spray mist drifting."

Personal Protective Equipment:

All labels should be amended to include the following recommendations for personal protective equipment:

> For mixing and loading:
> "Wear cotton coveralls and chemical-resistant gloves."

For application using the screened sprayer systems and for bagging/packing potatoes:

"Wear cotton coveralls and chemical-resistant gloves."

In facilities using closed fogger systems:

For all re-entry tasks (including cleaning) prior to the completion of ventilation:

"Wear chemical-resistant coveralls over a long-sleeved shirt and pants, chemical-resistant gloves and a self-contained breathing apparatus."

For cleaning following ventilation:

"Wear chemical-resistant coveralls over a long-sleeved shirt and pants, chemical-resistant gloves and a suitable respirator."

For tasks other than cleaning following ventilation:

"Wear cotton coveralls and chemical-resistant gloves."

RESTRICTED ENTRY INTERVAL:

Products that could potentially be used in large scale foggers must include following explicit label instructions regarding ventilation and restricted entry intervals:

"Do not allow entry into treated areas (to attend to fans, etc.) until two hours of mechanical ventilation (fans should circulate outside air) or four hours of passive ventilation (windows, vents and doors should be opened) have occurred."

PRECAUTIONS:

Remove the following statement:

"Do not feed treated potatoes to livestock."

DIRECTIONS FOR USE:

For Commercial Class products, the application rates must be expressed as volume or weight of product per 25, 50 or 100 tonnes of potatoes.